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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/563,616

08/09/2006

George F. Vande Woude

28927.0018

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277 7590 01/19/2011
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EXAMINER

GODDARD, LAURA B

ART UNIT

PAPER NUMBER

1642

MAIL DATE

DELIVERY MODE

01/19/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/563,616	Applicant(s) VANDE WOUDE ET AL.	
	Examiner LAURA B. GODDARD	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5,7-13,16-18,20-22,26,28-34,37,38 and 40-46 is/are pending in the application.
- 4a) Of the above claim(s) 9,10,13,16-18,22,26,28-34,37,38 and 41-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 7, 8, 11, 12, 20, and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date. _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Amendment filed November 3, 2010 in response to the Office Action of January 21, 2010, is acknowledged and has been entered. Claims 1, 5, 7-13, 16-18, 20-22, 26, 28-34, 37, 38, and 40-46 are pending. Claim 8 is amended. Claims 9, 10, 13, 16-18, 22, 26, 28-34, 37, 38, and 41-46 remain withdrawn. Claims 1, 5, 7, 8, 11, 12, 20, and 21 are currently being examined as drawn to the elected species of "TSP-1," "inhibitor of VEGF," and VEGF inhibitor "anti-VEGF antibody."

New Rejection

(based on new considerations)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1, 5, 7, 8, 11, 12, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al (Critical Reviews in Oncology Hematology, 2001, 39:155-171), in view of Sheibani et al (Histol Histolpathol, 1999, 14:285-294) and Streit et al (American J of Pathology, 1999, 155: 441-452, IDS).

Burke et al teach angiogenesis is required for the growth of tumors and metastasis (abstract) and suggest combining antiangiogenic agents with each other to target more than one mechanism of angiogenesis and produce synergistic combination

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therapy (abstract; p. 156, col. 1-2; Table 2). Burke et al teach RhuMAb VEGF (also known as bevacizumab) is a known antiangiogenic agent administered for cancer treatment and VEGF is a known contributor to angiogenesis and tumor growth (Table 1; p. 159, col. 1-2). Burke et al teach combination therapy with anti-VEGF therapy for cancer treatment (p. 159, col. 2 to p. 160, col. 1).

Burke et al do not teach administering a TSP-1 in combination with the VEGF inhibitor.

Sheibani et al teach upregulated angiogenesis contributes to cancer pathogenesis and is essential for tumor growth beyond a small nodule and for metastasis (p. 285, col. 2; p. 286, col. 2). Sheibani et al teach TSP1 is demonstrated to be a natural inhibitor of angiogenesis and inhibits angiogenesis *in vivo* (p. 286, col. 2). TSP1 also inhibits chemotactic migration of endothelial cells toward angiogenic factors such as FGFs, VEGF, PDGF, TGF- β , IL-8, and PGE1 (p. 287, col. 1).

Streit et al also teach that TSP-1 is a potent inhibitor of angiogenesis and tumor growth (abstract; p. 442, col. 1, first paragraph) and demonstrate TSP-1 gene transfection of tumor cells reduced tumor growth and angiogenesis *in vivo* (Figure 2C-F).

The references suggest the importance of anti-VEGF therapy, including bevacizumab, and TSP-1 in cancer and antiangiogenic treatment. However, the references are deficient in that they do not teach using these agents together. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use anti-VEGF agents or bevacizumab taught by Burke et al and TSP-1

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taught by Sheibani et al and Streit et al in combination in order to treat cancer and inhibit angiogenesis. One of ordinary skill in the art would have been motivated to use anti-VEGF agents (including bevacizumab) and TSP-1 in combination in a method of treating cancer in view of the importance of inhibiting angiogenesis that contributes to tumor growth and because Burke et al specifically suggest combining antiangiogenic agents with each other to target more than one mechanism of angiogenesis and produce synergistic combination therapy. Each of these agents had been taught by the prior art to be effective in the inhibition of angiogenesis and tumor growth, thus the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two modes of treatment, each of which is taught by the prior art to be useful for the same purpose in order to make a protocol that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims and composition claim, given the teaching of the prior art of processes using either anti-VEGF agents (including bevacizumab) or TSP-1 in the process of treating cancer and inhibiting angiogenesis, it would have been obvious to treat cancer with both anti-VEGF agents (including bevacizumab) and TSP-1 because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as agents for the same purpose of treating cancer by inhibiting angiogenesis. Further, one would have been motivated to combine bevacizumab and TSP-1 as antiangiogenic agents for therapy because Burke et al suggest combining antiangiogenic agents with

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each other to target more than one mechanism of angiogenesis and produce synergistic combination therapy. One of ordinary skill in the art would have reasonably expected to obtain effective treatment of cancer and inhibition of angiogenesis with either or both of these agents since both had been demonstrated in the prior art to successfully treat cancer by inhibiting angiogenesis.

3. All other rejections recited in the Office Action mailed January 21, 2010 are hereby withdrawn in view of amendments. The rejection of claims under 35 USC 102(e) and 103(a) are withdrawn in view of the declaration submitted under 37 CFR 1.131 (Woude and Zhang) demonstrating evidence for conceiving the claimed invention and reducing to practice prior to March 8, 2002, therefore disqualifying US Patent 7,351,729, Stein et al, and Rosen as prior art. Applicants' arguments are not drawn to the new rejection above.

4. **Conclusion:** No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642